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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,703	07/19/1999	STEPHEN A. JOBLING	CASE#1637	1158

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/297,703	Applicant(s) JOBLING ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,16-27 and 32* is/are pending in the application.

4a) Of the above claim(s) *3,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-8, 11, 16-27 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendments to claims 1-3, 6, 16-18 and 20-27 requested in Paper No. 20, filed 27 February, 2002, have been entered. Claims 1-11, 16-27 and 32 are pending.

2. Applicant, in the paper filed 27 February, 2002, again argues the restriction requirement, saying that Cooke et al taught an SBEI gene, while the instant invention is drawn to SBEII from cassava. This is not found persuasive. The originally presented claims were drawn to any SBE gene from any source. Thus, the restriction requirement remains FINAL.

Claims 3 and 9-10 are withdrawn from consideration, as being drawn to non-elected inventions. Applicant is required with delete non-elected sequences from all claims.

Claims 1-2, 4-8, 11, 16-27 and 32 are examined to the extent they read on SEQ ID NO:29.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The substitute specification filed 27 February, 2002, has been entered.

5. The drawings filed 28 January, 2002, are objected to for the reasons indicated on the accompanying form PTO 948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. See 37 CFR 1.85(a) and MPEP 608.02(b).

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from the specification (*e.g.*, pg 17, paragraph 1 of the specification filed 27 February, 2002) and the claims (claim 5).

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set for in this Office action will be held to be non-responsive.

Response to Amendment

7. The rejection of claims 1-2, 4-8, 11 and 32 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is WITHDRAWN in light of the amendments to claims 1 and 6 to indicate that nucleic acid is isolated.

8. The rejection of claims 1-2, 4-8, 11, 16-27 and 32 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility and under 35 U.S.C. 112, first paragraph is WITHDRAWN in light of the amendments to indicate that the nucleic acid encodes an SBE II enzyme.

9. The rejection of claims 1-2, 4, 6-8, 11 and 32 under 35 U.S.C. 102(b) as being anticipated by Burton et al is WITHDRAWN in light of the amendments to indicate that the nucleic acid encodes an SBE II enzyme.

10. The rejection of claims 1-2, 4, 6-8, 11, 16-17, 22-27 and 32 under 35 U.S.C. 103(a) as being unpatentable over Hofvander et al in view of Burton et al is WITHDRAWN in light of the amendments to indicate that the nucleic acid encodes an SBE II enzyme.

Claim Rejections - 35 USC § 112

11. Claims 1-2, 4-8, 11, 16-27 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:28 and nucleic

acids encoding SEQ ID NO:29, certain methods of using those nucleic acids, and plants transformed with those nucleic acids, does not reasonably provide enablement for other methods of using those nucleic acids, nor for nucleic acids encoding portions of SEQ ID NO:29 or that hybridize to SEQ ID NO:28 under conditions of unspecified stringency or that have 200 base pair regions with 88% identity to SEQ ID NO:28, methods of using those nucleic acids, and plants transformed with those nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the last Office action mailed 23 August, 2001.

Applicant's arguments filed 27 February, 2002, have been fully considered but they are not persuasive. Applicant urges that there is no undue experimentation needed to develop the methods of use and the plants so transformed. Applicant also urges that genetic manipulation and antisense technology are well known in the art, and that it would not be undue experimentation to test each variant claimed for their ability to suppress amylopectin formation. Applicant also argues that the specification provides guidance for which portions would be effective (*e.g.*, anything lacking the N-terminal up to the proline elbow) and provides several working examples. Applicant argues that it is well-established to conduct amino-acid alignments with homologous proteins to determine which regions are highly variable across species, and therefore able to tolerate substitutions, and which regions are highly conserved and thus critical to functionality. Applicant also argues that the relationship between homology and functionality is not consistent across all polypeptides and that plant enzymes are not as sensitive as growth factors. Applicant also argues that some guidance for substitutions is given in the specification. Applicant argues that the instant protein is 100 times longer that the seven amino acid changes

made by Broun et al and thus differs in the non-functional modifications that may be made. Applicant argues that Kossman et al did not know that there are two isoforms of SBE in potato and thus antisense exhibition of one of these would not be successful; furthermore, SBEII is the gene essential for modification. Applicant argues that Jobling et al showed that SBEII functionality is maintained in partial sequences (response pg 9-11).

This is not found persuasive. Applicant fails to point to page numbers of the specification where guidance is provided for making amino acid substitutions. Applicant also fails to provide support for the assertions that plant enzymes are not as sensitive to substitutions as growth factors.

In regards to Broun et al, a significant change was seen when substitutions were made in 4 out of 7 or 57% of the amino acids. This is a significant number regardless of how many amino acids are modified. Additionally, as discussed in the prior Office action, Hill et al made substitutions in three highly conserved histidines, which because they are highly conserved across a number of species, one would expect to tolerate either no change or only conservative substitutions. Unexpectedly, substitution with the "conservative" amino acid arginine drastically reduced enzyme activity while substitutions with a nonconservative amino acid did not. These results illustrate the unpredictability of making amino acid substitutions even when given a high level of guidance.

Given the lack of guidance provided by the specification and unpredictability associated with making amino acid substitutions, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding SBEII proteins or 200 bp long nucleic acids with 88% identity to SEQ ID NO:29. Making all possible single amino acid substitutions in an 836 amino acid long protein like that encoded by SEQ ID NO:28 would

require making and analyzing 19^{835} nucleic acids. Because 200 bp long nucleic acids encoding proteins with 88% identity to SEQ ID NO:29 would encode proteins with many more than a single amino acid substitution, nucleic acids with many substitutions would need to be made and analyzed.

The claims are not limited to portions lacking the N-terminal up to the proline elbow, but are broadly drawn to portions of any size.

While antisense suppression is a common method in the art, antisense constructs that are not completely homologous to the target gene are generally ineffective. As discussed in the prior Office action, Colliver et al showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with *increased* levels of chalcone synthase transcripts (pg 519, left column, paragraph 2) and note other instances when this phenomenon has occurred (pg 519, right column, paragraph 1).

Applicant is invited to submit a declaration presenting data that show that antisense suppression of SBEII in cassava or any other plant, using the gene of the instant invention, was successful in producing starch with altered properties.

12. Claims 1-2, 4-8, 11, 16-27 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the last Office action mailed 23 August, 2001.

Applicant's arguments filed 27 February, 2002, have been fully considered but they are not persuasive. Applicant urges that the claims have been amended to recite that the gene encodes SBEII.

This is not found persuasive because Applicant has not described the structural features of all nucleic acids that encode an "effective portion" of SEQ ID NO:29, that hybridize to any nucleic acid that encodes an "effective portion" of SEQ ID NO:29 under conditions of unspecified stringency, or that have 200 base pair regions with 88% identity to SEQ ID NO:28.

See *In re Shokal,* 113 USPQ 283, (CCPA 1957) at pg 285

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. ...
> We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

13. Claims 1-2, 4-8, 11, 16-27 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the last Office action mailed 23 August, 2001, as applied to claims 1-2, 4-8, 11, 16-27 and 32 and for the new reasons detailed below. Applicant's arguments filed 27 February, 2002, have been fully considered but they are not persuasive.

Claim 1 is indefinite for its recitation of "an effective portion." Applicant urges that the phrase is defined in the specification on pg 17, paragraphs 2 and 5 as a portion that retains SBE activity when expressed in *E. coli* KV832 to complement its branching mutation (response pg 12). This is not found persuasive. Pg 17, paragraphs 2 and 5 of the originally filed specification describes what the full-length cassava SBEII gene and cDNA encode, and pg 17, paragraphs 2

and 5 of the specification filed 27 February, 2002, describes isolation of an additional 740 bp of the gene by 5'RACE and that there is more than one SBE II gene in cassava. Neither is directed to a definition of "effective portion". Pg 3, paragraph 4 of the originally filed specification states that an "effective portion" MAY be defined as a portion that retains SBE activity when expressed in *E. coli* KV832. This does not constitute a definition of the term as "may" indicates that other definitions are contemplated. What those other definitions are remains unclear.

Claim 2 is indefinite for its recitation of "functionally equivalent nucleotide sequence". Applicant urges that the phrase has been amended out of the claim (response pg 12). This is not found persuasive because it has not been. It is not clear is this sequence encodes the same protein as that of SEQ ID NO:29, if it encodes a protein with the same enzymatic activity as that of SEQ ID NO:29, or if it simply encodes a protein.

The phrase "stringent hybridization conditions" in claim 2 is a relative phrase that renders the claims indefinite. Applicant urges that the phrase is defined on pg 4 of the specification (washing at 0.1xSSC, 0.5% SDS at 68 C). This is not found persuasive because the length of wash time and the hybridization conditions (salt concentration, percent SDS, time and temperature) are not described.

Claims 1, 6 and 26 are indefinite in their recitation of "having ... (SBEII) activity in cassava" and claim 16 is indefinite in their recitation of "having SBEII activity in cassava". It is unclear if Applicant means that the enzyme may be from any source but when placed in cassava has SBEII activity or is Applicant intended that the nucleic acid that encodes the enzyme be isolated from cassava. If the latter, it is suggested that "in cassava" be deleted and "from cassava" be inserted after "isolated nucleic acid" or "gene" or "polypeptide". With respect to claim 16, amendment may affect dependent claims, especially claim 17.

Claim Rejections - 35 USC § 102

14. Claims 1-2, 4 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Fisher et al (1996, GenBank Accession No. U22428 and Plant Mol. Biol. 30:97-108). The rejection is repeated for the reasons of record as set forth in the last Office action mailed 23 August, 2001.

Applicant's arguments filed 27 February, 2002, have been fully considered but they are not persuasive. Applicant urges that Fisher et al teaches an SBEII gene from maize while the present application discloses an SBEII gene from cassava, and that there is no evidence that the maize SBEII would have SBEII activity in cassava (response pg 14).

This is not found persuasive because the claims do not require that the nucleic acid be isolated from cassava, only that it would encode an SBEII if it were in cassava. As the vast majority of enzymes from one plant retain that activity when the gene encoding in is placed in another plant, it would be highly unlikely that the maize SBEII would not have SBEII activity in cassava. Additionally, the nucleic acid would encode an "effective portion" of SEQ ID NO:29 and would hybridize to SEQ ID NO:29 under "stringent conditions".

15. Claims 5-8, 16-27 and 32 are free of the prior art, given the failure of the prior art to teach or suggest isolated nucleic acids comprising at least 200 bp and having 88% identity to SEQ ID NO:29 and methods of suppressing in a plant both the SBEII and SBEI genes. Claim 5 is free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid that encodes a polypeptide with SBE activity, that encodes a portion of SEQ ID NO:28, and that

has the amino acid sequence Asn-Ser-Lys-His at about residue 697. Additionally, isolated nucleic acids encoding SEQ ID NO:29 are free of the prior art.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
May 14, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638